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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:21:55 ON 05 OCT 2007
L1             0 S CHOLESTRYL (W)ESTER (W)TRANSFERASE?
L2            64 S ESTER (W)TRANSFERASE?
L3       8648767 S CLON? OR EXPRESS? OR RECOMBINANT
L4            15 S L2 AND L3
L5            12 DUP REM L4 (3 DUPLICATES REMOVED)
L6             0 S "LIPAM-6"
L7          2983 S LIPID (W)ASSOCIATED
L8            24 S L7 AND TRANSFERASE?
L9             1 S L3 AND L8
                 E SARATOGA X J/AU
                 E JIAN X/AU
                 E JIANG X/AU
L10         3488 S E3
                 E BECHA S D/AU
L11          126 S E5
                 E YANG Y G/AU
L12          458 S E3
                 E SWARNAKER A/AU
L13            3 S E4
                 E BULLOCH S A/AU
L14           52 S E3-E6
L15         4093 S L10 OR L11 OR L12 OR L13 OR L14
L16            0 S L2 AND L15
L17            0 S L8 AND L15
L18           24 S L15 AND TRANSFERASE?
L19           17 DUP REM L18 (7 DUPLICATES REMOVED)

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NEWS	4	JUL 02	CHEMCATS accession numbers revised
NEWS	5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS	6	JUL 16	CAplus enhanced with French and German abstracts
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NEWS	14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
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NEWS	16	AUG 27	USPATOLD now available on STN
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NEWS	18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	19	SEP 13	FORIS renamed to SOFIS
NEWS	20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS	22	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	23	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	24	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt

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=> s cholestryl (w)ester (w)transferase?
L1             0 CHOLESTRYL (W) ESTER (W) TRANSFERASE?

=> s ester (w)transferase?
L2            64 ESTER (W) TRANSFERASE?

=> s clon? or express or recom,binant
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SEARCH ENDED BY USER

=> s clon? or express? or recombinant
L3       8648767 CLON? OR EXPRESS? OR RECOMBINANT

=> s l2 or l3
<------User Break------>

=> s l2 and l3
L4            15 L2 AND L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            12 DUP REM L4 (3 DUPLICATES REMOVED)

=> d 1-12 ibib ab
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L5 ANSWER 1 OF 12 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 1
ACCESSION NUMBER: 2005-20729 BIOTECHDS
TITLE: Novel isolated peptide comprising amphipathic alpha helix, and having cholesterol efflux mediating and ATP-binding cassette transporter A stabilization activity, useful for treating diseases associated with dyslipidemia e.g. stroke; vector-mediated gene transfer and expression in host cell for recombinant apolipoprotein production for use in disease therapy
AUTHOR: BIELICKI J K; NATARAJAN P
PATENT ASSIGNEE: UNIV CALIFORNIA
PATENT INFO: WO 2005058938 30 Jun 2005
APPLICATION INFO: WO 2004-US42251 15 Dec 2004
PRIORITY INFO: US 2003-529933 15 Dec 2003; US 2003-529933 15 Dec 2003
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2005-479315 [48]
AB DERWENT ABSTRACT:

NOVELTY - An isolated peptide comprising an amphipathic alpha helix comprising 18 or more amino acids, a polar face and a nonpolar face, where the helix is from a protein chosen from Apo A-I, Apo A-II, Apo A-IV, Apo E, Apo C-I, Apo C-II, Apo C-III, serum amyloid A, and their combinations, and having a cholesterol efflux mediating activity and an ATP-binding cassette transporter A (ABCA) stabilization activity, is new.

DETAILED DESCRIPTION - An isolated peptide (I), comprises an amphipathic alpha helix comprising 18 or more amino acids, a polar face and a nonpolar face, where the polar face comprises an alignment of at least 3 acidic amino acids positioned at every 2-3 helical turns, and the helix is from a protein chosen from Apo A-I, Apo A-II, Apo A-IV, Apo E, Apo C-I, Apo C-II, Apo C-III, serum amyloid A and their combinations, and has a cholesterol efflux mediating activity and an ATP-binding cassette transporter A (ABCA) stabilization activity. INDEPENDENT CLAIMS are also included for: (1) a pharmaceutical composition (II) comprising (I) and a carrier; (2) an isolated nucleic acid (III) encoding (I); (3) an expression vector (IV) comprising (III); (4) a host cell (V) comprising (IV); (5) making (M1) a non-naturally occurring peptide having a cholesterol efflux activity, involves identifying an amphipathic alpha helix peptide comprising a polar face and a nonpolar face in a protein chosen from Apo A-I, Apo A-II, Apo A-IV, Apo E, Apo C-I, Apo C-II, Apo C-III, and serum amyloid A, where the amphipathic alpha helix peptide comprises between 10 and 200 amino acids, modifying the polar face of the helix peptide to comprise an alignment of at least three acidic amino acids positioned at every 2-3 helical turns to create a modified helix peptide, selecting a modified helix peptide that has at least twice the cholesterol efflux mediating activity as the amphipathic alpha helix peptide and synthesizing the modified helix peptide, or identifying a first and second amphipathic alpha helix peptides in a protein chosen from Apo A-I, Apo A-II, Apo A-IV, Apo E, Apo C-I, Apo C-II, Apo C-III, and serum amyloid A, where the amphipathic alpha helix peptide comprises between 10 and 200 amino acids, linking the first and second amphipathic alpha helix peptides to form an alignment of acidic, where the acidic amino acids are positioned at every 2-3 helical turns to create a modified helix peptide, and carrying out selecting and synthesizing steps mentioned above; and (6) making (M2) a non-naturally occurring peptide having an ABCA stabilization activity, involves carrying out the steps of (M1), where the selection step involves selecting a modified helix peptide that has at least twice the ABCA stabilization activity has the amphipathic alpha helix peptide.

BIOTECHNOLOGY - Preferred Peptide: (I) comprises at least one amino acid substitution to create the alignment of acidic amino acids. The ABCA is chosen from ABCA1 and ABCA7. (I) has an antioxidant activity, where one or more native amino acid residue at or near the polar/nonpolar

interface of the amphipathic alpha helix is substituted with a cysteine. (I) has an anti-inflammatory activity. (I) comprises at least one D amino acid, preferably the carboxy terminus and the amino terminus comprises a D amino acid and most preferably all D amino acids. The helix comprises a sequence chosen from helix 1 (amino acids 44-65) of Apo A-I, helix 6 (amino acids 145-162) of Apo A-I, helix 7 (amino acids 167-184) of Apo A-I, helix 9 (amino acids 209-219) of Apo A-I, helix 10 (amino acids 220-238) of Apo A-I, amino acids 1-51 or 5-32 of Apo A-II, amino acids 62-94, 66-90, 183-204, 183-226, 205-226, 161-204, 161-182, 205-248, 227-248, 117-138 or 138-160 of Apo A-IV, amino acids of 25-57, 6-27 or 29-53 of Apo C-I, amino acids 12-42, 16-40 or 43-68 of Apo C-II, amino acids 37-69 or 45-69 of Apo C-III, the C terminal domain (amino acids 216-299) of Apo E, amino acids 216-248, 216-237, 238-266, 267-299 or 238-263 of Apo E, and amino acids 1-36, 1-34, 5-29 or 53-78 of serum amyloid A. (I) comprises a sequence chosen from one of 41 fully defined amino acid 22-55 amino acid sequences (SEQ ID Number 1-41) given in the specification. (I) further comprises a second amphipathic alpha helix comprising an alignment of acidic amino acids, where the acidic amino acids are positioned at every 2-3 helical turns, the second helix is from a protein chosen from Apo A-I, Apo A-II, Apo A-IV, Apo E, Apo C-I, Apo C-II, Apo C-III, serum amyloid A, and their combinations, and (I) has a cholesterol efflux mediating activity and an ABCA stabilization activity. The first and the second amphipathic helices comprise a sequence chosen from helix 1 (amino acids 44-65) of Apo-I and helix 9 (amino acids 209-219) of Apo A-I linked in order, helix 9 (amino acids 209-219) of Apo A-I and helix (amino acids 44-65) of Apo A-I linked in order, helix 6 (amino acids 145-162) of Apo A-I and helix 10 (amino acids 220-238) of Apo A-I linked in order, helix 7 (amino acids 167-184) of Apo A-I and helix 10 (amino acids 220-238) of Apo A-I linked in order, helix 9 (amino acids 201-219) of Apo A-I and helix 10 (amino acids 220-238) of Apo A-I linked in order, helix 6 (amino acids 145-162) of Apo A-I and helix 7 (amino acids 167-184) of Apo A-I linked in order, helix 1 (amino acids 44-65) of Apo A-I and helix 2 (amino acids 66-87) of Apo A-I linked in order, helix 8 (amino acids 185-209) of Apo A-I and helix 10 (amino acids 220-238) of Apo A-I linked in order, and the C terminal domain of Apo E (amino acids 216-299). Preferred Composition: (II) further comprises a therapeutic agent for treating cardiovascular disease, where the therapeutic agent is chosen from a statin, bile acid binder, platelet clumping inhibitor, nicotinamide, peroxisome proliferative activated receptor (PPAR) agonists, vitamin E, a cholesterol ester transferase protein (CETP) inhibitor, an angiotensin converting enzyme (ACE) inhibitor, a beta blocker, and their combinations. Preferred Method: In (M1) and (M2), the modified helix peptide comprises at least one D amino acid. The carboxy terminus of and the amino terminus of the modified helix peptide comprises a D amino acid. The modified helix peptide comprises all D amino acids. (M1) further involves substituting at least one native amino acid residue at or near the polar/nonpolar interface of the modified helix peptide with a cysteine.
Pro-Ala-Leu-Glu-Asp-Leu-Arg-Gln-Gly-Leu-Leu-Pro-Val-Leu-Glu-Ser-Phe-Cys-Val-Lys-Phe-Leu-Ser-Ala-Leu-Glu-Glu-Tyr-Thr-Lys-Lys-Leu-Asn (SEQ ID Number 1) Pro-Val-Leu-Glu-Ser-Phe-Lys-Val-Ser-Phe-Leu-Ser-Ala-Leu-Glu-Glu-Tyr-Lys-Thr-Lys-Leu-Glu-Ser-Ala-Leu-Asn (SEQ ID Number 2) Ala-Arg-Met-Glu-Glu-Met-Gly-Ser-Arg-Thr-Arg-Asp-arg-Leu-Asp-Glu-Val-Lys-Glu-Gln-Val-Ala-Glu-Val-Arg-Ala-Lys-Leu-Glu-Glu-Gln-Ala-Gln-Gln-Ile-Arg-Leu-Gln-Ala-Glu-Ala-Phe-Gln-Ala-Arg-Leu-Lys-Ser-Trp-Phe-Glu-Pro-Leu-Val-Glu (SEQ ID Number 4) Ala-Arg-Met-Glu-Glu-Met-Gly-Ser-Arg-Thr-Arg-Asp-Arg-Leu-Asp-Glu-Val-Lys-Glu-Gln-Val-Ala (SEQ ID Number 7) Pro-His-Ala-Asp-Glu-Leu-Lys-Ala-Lys-Ile-Asp-Gln-Asn-Val-Glu-Glu-Leu-Lys-Gly-Arg-Leu-Thr (SEQ ID Number 14) Thr-Gln-Val-lys-Glu-Ser-Leu-Ser-Ser-Tyr-Trp-Glu-Ser-Ala-Lys-Thr-Ala-Ala-Gln-Asn-Leu-Tyr-Glu-Lys-Thr (SEQ ID Number 26) Gln-Ala-Lys-Glu-Pro-Cys-Val-Glu-Ser-Leu-Val-Ser-Gln-Tyr-Phe-Gln-Thr-Val-Thr-Asp-Tyr-Gly-Lys-Asp-Leu-Met-Glu-Lys-Val-Lys-Ser-Pro-Glu-Leu-Gln-Ala-Glu-Ala-Lys-Ser-Tyr-Phe-Glu-Lys-Ser-Lys-Glu-Gln-Leu-Thr-Pro (SEQ ID Number 30) Arg-Ser-Phe-Phe-Ser-Phe-Leu-Gly-Glu-Ala-Phe-Asp-Gly-Ala-Arg-Asp-Met-Trp-Arg-Ala-Tyr-Ser-Asp-Met-

Arg-Glu-Ala-Asn-Tyr-Ile-Gly-Ser-Asp-Lys (SEQ ID Number 33) Trp-Ala-Ala-Glu-Val-Ile-Ser-Asn-Ala-Arg-Glu-Asn-Ile-Gln-Arg-Leu-Thr-Gly-His-Gly-Ala-Glu-Asp-Ser-Leu-Ala (SEQ ID Number 35) Leu-Lys-Leu-Leu-Asp-Asn-Trp-Asp-Ser-Val-Thr-Ser-Thr-Phe-Ser-Lys-Leu-Arg-Glu-Gln-Leu-Gly-Pro-Ala-Leu-Glu-Asp-Leu-Arg-Gln-Gly-Leu-Leu (SEQ ID Number 37) Pro-Ala-Leu-Glu-Asp-Arg-Gln-Gly-Leu-Leu-Leu-Lys-Leu-Leu-Asp-Asn-Trp-Asp-Ser-Val-Thr-Ser-Thr-Phe-Ser-Lys-Leu-Arg-Glu-Gln-Leu-Gly (SEQ ID Number 41)

ACTIVITY - Cardiant; Antiarteriosclerotic; Cerebroprotective; Vasotropic; Neuroprotective; Nootropic.

MECHANISM OF ACTION - Mediator of cholesterol efflux (claimed). No biological data given.

USE - (I) is useful for mediating cholesterol efflux in a mammalian subject, which involves administering (I) to the subject (claimed). (I) or (II) is useful for treating, preventing or diagnosing diseases and disorders associated with dyslipidemia such as heart disease, artherosclerotic lesions, stroke, Alzheimer's disease and storage disorders.

ADMINISTRATION - Administration of (II) is by oral, intravenous, transdermal or rectal route, or by injection or inhalation, at a dosage ranging from 0.1-50 mg/kg body weight, preferably 1-25 and most preferably 1-20 mg/kg body weight.

EXAMPLE - No suitable example given.(126 pages)

L5 ANSWER 2 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:169905 BIOSIS
DOCUMENT NUMBER: PREV200500175978
TITLE: Shuttling between species for pathways of lifespan regulation: a central role for the vitellogenin gene family?.
AUTHOR(S): Brandt, Bernd W. [Reprint Author]; Zwaan, Bas J.; Beekman, Marian; Westendorp, Rudi G. J.; Slagboom, P. Eline
CORPORATE SOURCE: Med CtrDept Med Stat and BioinformatSect Mol Epidemiol, Leiden Univ, POB 9503, NL-2300 RA, Leiden, Netherlands b.w.brandt@lumc.nl
SOURCE: BioEssays, (March 2005) Vol. 27, No. 3, pp. 339-346. print. ISSN: 0265-9247 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: DDBJ-AAC02607; EMBL-AAC02607; GenBank-AAC02607; NCBI-CG9342; NCBI-KOG4337
ENTRY DATE: Entered STN: 4 May 2005
Last Updated on STN: 4 May 2005

L5 ANSWER 3 OF 12 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN

ACCESSION NUMBER: 2004-12746 BIOTECHDS
TITLE: Using atomic coordinates of bactericidal/permeability-increasing protein for modeling bactericidal/permeability-increasing protein and its related lipid transfer protein and designing a model of ligands; recombinant protein production via plasmid expression in host cell for use in disease therapy
AUTHOR: BEAMER L J; CARROLL S F; EISENBERG D; KLEIGER G
PATENT ASSIGNEE: BEAMER L J; CARROLL S F; EISENBERG D; KLEIGER G
PATENT INFO: US 2004014153 22 Jan 2004
APPLICATION INFO: US 2002-162743 5 Jun 2002
PRIORITY INFO: US 2002-162743 5 Jun 2002; US 1997-879565 20 Jun 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-224231 [21]
AB DERWENT ABSTRACT:
NOVELTY - Using (M1) atomic coordinates of bactericidal/permeability-increasing (BPI) protein or its fragment, analog or variants, for modeling BPI protein and a BPI-related lipid transfer protein (I), designing a chemical compound capable of associating with (I), designing

a model of ligands, and for designing compounds with an activity such as antibacterial, antifungal, antimycobacterial, is new.

DETAILED DESCRIPTION - Using (M1) atomic coordinates of bactericidal/permeability-increasing (BPI) protein or its fragment, analog or variants, for modeling BPI protein and a BPI-related lipid transfer protein (I), computationally designing a chemical compound for mimicking a BPI protein and (I) or its fragment, analog or variant, designing a chemical compound capable of associating with (I) or its fragment, analog or variant, designing a model of ligands in an active site of a lipid binding protein, and for designing compounds with an activity such as antibacterial, antifungal, antimycobacterial, antichlamydial, antiprotozoan, heparin-binding, endotoxin-binding, heparin-neutralizing, endotoxin-neutralizing, inhibition of tumor or endothelial cell proliferation, inhibition of angiogenesis, anti-inflammatory, anticoagulant, antithrombolytic, enhancement of pericyte cell proliferation, enhancement of antibiotic activity or susceptibility, or inhibition of H+/K+ ATPase activity. INDEPENDENT CLAIMS are also included for: (1) three-dimensional modeling of a BPI protein or (I) involves providing three-dimensional atomic coordinates derived from X-ray diffraction measurements of a BPI protein in a computer readable format, inputting the obtained data into a computer with appropriate software program, and generating a three-dimensional structural representation of the BPI protein or (I) suitable for visualization and further computational manipulation; (2) providing (M2) an atomic model of a BPI protein, or its fragment, analog or variant comprising: (a) providing a computer readable medium (CRM) having stored its atomic coordinate/X-ray diffraction data of the BPI protein, or its fragment, analog or variant, in crystalline form, where the data is sufficient to model the three-dimensional structure of the BPI protein, or its fragment, analog or variant; (b) analyzing on a computer using a subroutine executed in the computer, atomic coordinate/X-ray diffraction data from (a) to provide atomic coordinate data output defining an atomic model of the BPI protein, or its fragment, analog or variant, where analyzing utilizes a computing algorithm or computing subroutine (II) chosen from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement and positional refinement; and (c) obtaining atomic coordinate data (III) defining the three-dimensional structure of a BPI protein, or its fragment, analog or variant; (3) a computer-based system for providing atomic model data of the three-dimensional structure of BPI protein, or its fragment, analog or variant, a BPI mutant or a BPI fragment comprising the following elements: CRM having stored atomic coordinate/X-ray diffraction data of the BPI protein, or its fragment, analog or variant, a computing subroutine that when executed in a computer causes the computer to analyze atomic coordinate/X-ray diffraction data from the above step, to provide atomic coordinate data output defining an atomic model of the BPI protein, or its fragment, analog or variant, where analyzing utilizes one of (II), retrieval unit for obtaining (III); (4) providing (M3) a computer atomic model of a ligand of a BPI protein, or its fragment, analog or variant involves providing CRM having stored atomic coordinate data of a BPI protein, or its fragment, analog or variant, providing a CRM having stored atomic coordinate data sufficient to generate atomic models of potential ligands of the BPI protein, or its fragment, analog or variant, analyzing on a computer using a subroutine executed in the computer, atomic coordinate data and ligand data from the above, to determine binding sites of BPI protein, or its fragment, analog or variant, and to provide atomic coordinate data defining an atomic model of a ligand of the BPI, BPI mutant or its fragment, where the analyzing utilizes one of (II), and obtaining atomic coordinate model output data defining the three-dimensional structure of a ligand of the BPI protein, or its

fragment, analog or variant; and (5) a computer-based system for (M3) comprises a CRM having (III), a CRM having stored atomic coordinate data sufficient to generate atomic models of potential ligands of a BPI, mutant or its fragment, a (II) for analyzing on a computer the atomic coordinate data from the above steps, to determine binding sites of BPI protein, or its fragment, analog, or variant, and to provide data output defining an atomic model of a potential ligand of BPI protein, or its fragment, analog or variant, and retrieval unit for obtaining (III).

WIDER DISCLOSURE - The following are also disclosed as new: (1) expressing, purifying and crystallizing BPI products; and (2) mutants of BPI or its fragments, analog or variants.

BIOTECHNOLOGY - Preferred Method: In (M1), (I) is lipopolysaccharide-binding protein (LBP), cholesteryl ester transferase protein (CETP) or phospholipid transfer protein (PLTP), or its fragment, analog or variant. The BPI protein comprises a binding site comprising an amino acid sequence, or variant of the sequence chosen from positions 17-45, 36-54, 65-99, 84-109, 142-164, or 142-169 of BPI. The BPI protein comprises a binding site containing amino acid residues of a binding pocket as given in the specification, e.g., Val, Ile, Gly at positions 7, 9, 13 respectively, in the amino acid sequence of BPI protein. The lipid binding protein is BPI, LBP, CETP or PLTP, or its fragment, analog or variant. The atomic coordinates of BPI protein are given in the specification. In (M2), the CRM further has stored data corresponding to a nucleic acid sequence or amino acid sequence data comprising a structural domain or functional domain of a BPI, LBP, CETP or PLTP corresponding to a BPI or mutant primary sequence of 456, 456, 476 or 470 amino acids respectively as given in the specification or its fragment, where the analyzing step further comprises analyzing the sequence data.

ACTIVITY - Antibacterial; Fungicide; Protozoacide; Cytostatic; Antiinflammatory; Anticoagulant; Antiangiogenic; Thrombolytic. No biological data given.

MECHANISM OF ACTION - None given.

USE - (M1) uses the atomic coordinates of BPI protein or its fragment, analog or variants, for modeling BPI protein and (I), computationally designing a chemical compound for mimicking a BPI protein and (I) or its fragment, analog or variant, designing a chemical compound capable of associating with (I) or its fragment, analog or variant, designing a model of ligands in an active site of a lipid binding protein, and for designing compounds with an activity such as antibacterial, antifungal, antimycobacterial, antichlamydial, antiprotozoan, heparin-binding, endotoxin-binding, heparin-neutralizing, endotoxin-neutralizing, inhibition of tumor or endothelial cell proliferation, inhibition of angiogenesis, anti-inflammatory, anticoagulant, antithrombolytic, enhancement of pericyte cell proliferation, enhancement of antibiotic activity or susceptibility, or inhibition of H+/K+ ATPase activity. (all claimed).

EXAMPLE - The plasmid pIC108 containing a cDNA encoding bactericidal/permeability-increasing (BPI) cloned in a T3T7 plasmid served as the starting point for the construction of a vector for expression of non-glycosylated rBPI in mammalian cells. A unique XhoI site was first added to the 3' end of the BPI gene in pIC108. Two oligonucleotides were synthesized for this purpose: BPI-53 (5' actggttccatggaggtcagcgcc 3') encoding amino acids 361-370 of BPI-54 (5' gacagatctctcgagtcatttatagacaa 3') encoding the last four amino acids of coding sequence, the stop codon (TGA), and incorporating an XhoI site immediately downstream of the stop codon. These oligonucleotides were used to PCR amplify a 280 base pair (bp) fragment of the C-terminus of BPI and incorporate the XhoI site at the 3' end of the gene. The amplified fragment was digested with NcoI and BgIII and ligated to approximately 4100 bp NcoI-BamHI fragment from pIC108 to generate the plasmid pSS101. The glycosylation site was next removed by replacing the region from a unique XcmI site to a unique SphI site within the BPI gene in pSS101 with an annealed oligonucleotide that contained the codon (TCC)

for the serine at amino acid position 351 changed to the codon (GCC) for alanine. pSS102 was digested with BstBI and XhoI and a 596 bp fragment, which included the modified BPI sequence, was purified and ligated to the large BstBI-XhoI fragment from pING4147 which contains the gpt gene encoding resistance to mycophenolic acid, the human Ig enhancer, the human cytomegalovirus promoter (CMV) and the mouse light chain 3' untranslated region and is identical to the vector, pING4144. Chinese hamster ovary (CHO)-K1 cells were transfected by electroporation with 40 microg of pING4322. Transfected CHO-K1 host cells were cultivated in roller bottles for three days, after three days fresh media DME/F12 with 2.5 % fetal bovine serum (FBS) was added with a 10 ml slurry of sterilized S-Sepharose and 1 ml of 1 M solution of sodium butyrate. After 2 days, the S-Sepharose was removed and the expressed non-glycosylated rBPI protein was purified from the pooled S-Sepharose. The purified protein was filtered and was crystallized by hanging-drop vapor diffusion at room temperature. The protein concentration was 8.5 mg/ml and the crystallization buffer contained 12 % (w/v) PEG 8000, 200 mM magnesium acetate, and 100 mM sodium cacodylate, pH 6.8. The crystal forms obtained showed a crystal structure of BPI and two bound phospholipids at 2.4 Angstrom resolution. The overlapping BPI peptide data showed that the N-terminal domain of BPI contains at least three independent functional domains that have one or more biological activities of BPI. (168 pages)

L5 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:408765 HCAPLUS
DOCUMENT NUMBER: 137:1501
TITLE: Enzymes of 3-hydroxypropionic acid metabolism and their use in the manufacture of 3-hydroxypropionic acid metabolites and their polymers
INVENTOR(S): Gokarn, Ravi R.; Selifonova, Olga V.; Jessen, Holly; Gort, Steven J.; Selmer, Thorsten; Buckel, Wolfgang
PATENT ASSIGNEE(S): Cargill, Incorporated, USA
SOURCE: PCT Int. Appl., 237 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042418	A2	20020530	WO 2001-US43607	20011120
WO 2002042418	A9	20021121		
WO 2002042418	A3	20030626		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2429039	A1	20020530	CA 2001-2429039	20011120
AU 200219818	A	20020603	AU 2002-19818	20011120
EP 1343874	A2	20030917	EP 2001-997539	20011120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015877	A	20031007	BR 2001-15877	20011120
JP 2004514431	T	20040520	JP 2002-545124	20011120
CN 1556855	A	20041222	CN 2001-821785	20011120
AU 2002219818	B2	20070816	AU 2002-219818	20011120

MX 2003PA04324	A	20040126	MX 2003-PA4324		20030516
US 2004076982	A1	20040422	US 2003-432443		20031020
US 7186541	B2	20070306			
US 2007184524	A1	20070809	US 2006-539856		20061009
PRIORITY APPLN. INFO.:			US 2000-252123P	P	20001120
			US 2001-285478P	P	20010420
			US 2001-306727P	P	20010720
			US 2001-317845P	P	20010907
			WO 2001-US43607	W	20011120
			US 2003-432443	A3	20031020

AB Microbial enzymes and accessory proteins involved in the metabolism of 3-hydroxypropanoic acid (3HP) are identified and genes encoding them cloned and characterized for use in the manufacture of metabolites and their polymers. The gene for propionyl-CoA transferase was cloned from Megasphaera elsdenii by PCR using degenerate primers derived from conserved regions of known CoA ester transferases followed by genome walking to obtain full-length genes. The enzyme accepted a broad range of CoA esters as substrates. Similarly, genes for related enzymes, lactyl-CoA dehydratase and 3-hydroxypropionyl-CoA dehydratase and their activator proteins were cloned. Operons containing these genes were constructed using the expression vector pET11a and introduced into Escherichia coli. E. coli carrying these constructs was able to synthesize lactic acid and 3HP.

L5 ANSWER 5 OF 12 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000283591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10748193
TITLE: A broad role for the zinc finger protein ZNF202 in human lipid metabolism.
AUTHOR: Wagner S; Hess M A; Ormonde-Hanson P; Malandro J; Hu H; Chen M; Kehrer R; Frodsham M; Schumacher C; Beluch M; Honer C; Skolnick M; Ballinger D; Bowen B R
CORPORATE SOURCE: Myriad Genetics, Inc., Salt Lake City, Utah 84108 and Novartis Institute for Biomedical Research, Summit, New Jersey 07901, USA.. swagner@myriad.com
SOURCE: The Journal of biological chemistry, (2000 May 26) Vol. 275, No. 21, pp. 15685-90.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 14 Jul 2000
Last Updated on STN: 14 Jul 2000
Entered Medline: 30 Jun 2000

AB The ZNF202 gene resides in a chromosomal region linked genetically to low high density lipoprotein cholesterol in Utah families. Here we show that the ZNF202 gene product is a transcriptional repressor that binds to elements found predominantly in genes that participate in lipid metabolism. Among its targets are structural components of lipoprotein particles (apolipoproteins AIV, CIII, and E), enzymes involved in lipid processing (lipoprotein lipase, lecithin cholesteryl ester transferase), and several genes involved in processes related to energy metabolism and vascular disease. Based on the linkage and apparent transcriptional function of ZNF202, we propose that ZNF202 is a candidate susceptibility gene for human dyslipidemia.

L5 ANSWER 6 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:112152 BIOSIS
DOCUMENT NUMBER: PREV200100112152
TITLE: Marked reduction in early atherosclerosis in cholesterol-fed human cholesterol ester transfer protein transgenic (hCETP-Tg) mice.

AUTHOR(S): Jimi, Shiro [Reprint author]; Shimoji, Eisou [Reprint author]; Zhang, Bo [Reprint author]; Saku, Keijiro [Reprint author]
CORPORATE SOURCE: Fukuoka Univ, Fukuoka, Japan
SOURCE: Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.89. print.
Meeting Info.: Abstracts from American Heart Association Scientific Sessions 2000. New Orleans, Louisiana, USA. November 12-15, 2000. American Heart Association.
CODEN: CIRCAZ. ISSN: 0009-7322.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Feb 2001
Last Updated on STN: 15 Feb 2002

L5 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:641024 HCAPLUS
DOCUMENT NUMBER: 131:270100
TITLE: Silent and missense single nucleotide polymorphisms in genes associated with vascular disease and their uses
INVENTOR(S): Lander, Eric S.; Daley, George Q.; Cargill, Michele; Ireland, James S.; Rozen, Steven G.
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950454	A2	19991007	WO 1999-US6473	19990326
WO 9950454	A3	20000413		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6692909	B1	20040217	US 1998-54272	19980401
CA 2324285	A1	19991007	CA 1999-2324285	19990326
AU 9933638	A	19991018	AU 1999-33638	19990326
EP 1068353	A2	20010117	EP 1999-915022	19990326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-54272 A2 19980401
WO 1999-US6473 W 19990326

AB Silent and missense mutations arising from single nucleotide polymorphisms in the coding regions of genes associated with vascular function and vascular disease are described. Allele-specific primers and probes hybridizing to regions flanking or containing these sites are also provided. The polymorphisms, primers and probes are used in applications such as phenotype correlations, forensics, paternity testing, medicine and genetic anal.

L5 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:282118 HCAPLUS
DOCUMENT NUMBER: 130:310673

TITLE: Xenogeneic cholesteryl ester transfer protein (CETP) for modulation of CETP activity in treatment of atherosclerosis
INVENTOR(S): Rittershaus, Charles W.; Thomas, Lawrence J.
PATENT ASSIGNEE(S): Avant Immunotherapeutics, Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920302	A1	19990429	WO 1998-US22145	19981020
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2307012	A1	19990429	CA 1998-2307012	19981020
AU 9911048	A	19990510	AU 1999-11048	19981020
AU 747709	B2	20020523		
EP 1024825	A1	20000809	EP 1998-953762	19981020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001520204	T	20011030	JP 2000-516697	19981020
PRIORITY APPLN. INFO.:			US 1997-954643 A2	19971020
			WO 1998-US22145 W	19981020

AB Methods for modulating cholesteryl ester transfer protein (CETP) activity and the plasma levels of lipoproteins involved in heart disease involve administration of a non-endogenous CETP or a plasmid-based vaccine for expression of such non-endogenous CETP to elicit production in a mammal of antibodies that recognize (bind to) the mammal's native (endogenous) CETP.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 12 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1998-01600 BIOTECHDS
TITLE: DNA plasmid based vaccine;
nucleic acid vaccine for cardiovascular disease
AUTHOR: Thomas L J
PATENT ASSIGNEE: T-Cell-Sci.
LOCATION: Needham, MA, USA.
PATENT INFO: WO 9741227 6 Nov 1997
APPLICATION INFO: WO 1997-US7294 1 May 1997
PRIORITY INFO: US 1997-802967 21 Feb 1997; US 1996-640713 1 May 1996
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1997-549731 [50]
AB A new nucleic acid vaccine comprises a DNA sequence (I) encoding an immunogenic protein, where at least 1 segment of (I) encodes a B-lymphocyte epitope of cholesterylester-transferase protein (CETP) linked with at least 1 segment encoding a broad range helper T-lymphocyte epitope, where the nucleotide segment is operably linked to a promoter for directing transcription of (I) in a mammalian cell. Also claimed are: a DNA based plasmid vaccine comprising a nucleotide sequence comprising the immediate early promoter/enhancer region of cytomegalo virus operably linked to a structural DNA segment encoding an immunogenic protein selected from preferred regions of a disclosed protein sequence;

a DNA plasmid-based vaccine comprising a DNA segment encoding a broad range T-lymphocyte epitope. The nucleic acid vaccine can be used to elevate the ratio of circulating high density lipoproteins to circulating low density lipoproteins, very low density lipoproteins or total cholesterol in a human and for reducing the level of endogenous CETP activity in a human. The vaccine can also be used to induce antibodies and for cardiovascular disease therapy. (67pp)

L5 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:493073 HCAPLUS
DOCUMENT NUMBER: 119:93073
TITLE: Cholesteryl ester transfer protein deficiency caused by a nonsense mutation detected in the patient's macrophage mRNA
AUTHOR(S): Gotoda, Takanari; Kinoshita, Makoto; Shimano, Hitoshi; Harada, Kenji; Shimada, Masako; Ohsuga, Junichi; Teramoto, Tamio; Yazaki, Yoshio; Yamada, Nobuhiro
CORPORATE SOURCE: Fac. Med., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Biochemical and Biophysical Research Communications (1993), 194(1), 519-24
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cholesteryl ester transfer protein (CETP) deficiency causes marked elevation of plasma high-d. lipoproteins, termed hyperalphalipoproteinemia. Only one CETP mutation has been found previously, partly because the relative unavailability of CETP mRNA has hampered anal. The authors demonstrated CETP mRNA expression in macrophages and identified a new CETP mutation by analyzing the macrophage mRNA of a homozygous patient with a familial form of hyperalphalipoproteinemia. The nonsense mutation at codon 309 in exon 10 of the CETP gene was thought to delete the carboxy-terminal third and caused a decrease in the level of CETP mRNA. These findings provide more evidence that CETP mutations may underlie a subset of familial hyperalphalipoproteinemia.

L5 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:2903 HCAPLUS
DOCUMENT NUMBER: 118:2903
TITLE: Nucleotide and deduced amino acid sequences of the oxidosqualene cyclase from Candida albicans
AUTHOR(S): Buntel, Christopher J.; Griffin, John H.
CORPORATE SOURCE: Dep. Chem., Stanford Univ., Stanford, CA, 94305-5080, USA
SOURCE: Journal of the American Chemical Society (1992), 114(24), 9711-13
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The DNA and predicted amino acid sequence of the oxidosqualene-lanosterol cyclase from the fungus Candida albicans is reported. This work was undertaken as the initial step in a program of reached directed at elucidating in detail the structural and functional basis for enzymic catalysis of polyene cyclization reactions. Portions of C. albicans genomic DNA sequences found by R. Kelly et al. (1990) to complement cyclase-deficient Saccharomyces cerevisiae mutants were subcloned and sequenced using the Sanger dideoxy chain-termination technol. This revealed an open reading frame of 2187 nucleotides (including stop codon) which is predicted to encode a 728 amino acid, 83.7 kDa protein. Consensus TATA box promoter and polyadenylation signal sequences were observed before the initiation codon and after the stop codon, resp. A search of the GenBank 71 and EMBL DNA sequence databases revealed no significant homologies to known gene sequences. A search of the PIR 31 and SWISS-PROT 21 protein sequence databases revealed a limited similarity

to the human cholesteryl ester transferase. Direct comparison with the predicted amino acid sequence of the squalene-hopene cyclase from Bacillus acidocaldarius recently reported by D. Ochs et al. (1992) reveals four regions of substantial similarity, ranging from 29% identity over 77 residues to 46% identity over 37 residues. The C. albicans cyclase is predicted to have two notably hydrophobic regions which may be involved in the expected membrane localization by this enzyme. Both the C. albicans and B. acidocaldarius cyclases have regions of primary sequence rich in tryptophan and/or tyrosine residues. The electron-rich aromatic sidechains of some of these residues may serve to stabilize cationic transition states and/or high-energy intermediates along the cyclization/rearrangement pathway.

L5 ANSWER 12 OF 12 EMBASE

ACCESSION NUMBER: 1987082942 EMBASE
TITLE: A hyperalphalipoproteinaemic family with normal cholesteryl ester transfer/exchange activity.
AUTHOR: Groener J.E.M.; Da Col P.G.; Kostner G.M.
CORPORATE SOURCE: Institute of Medical Biochemistry, University of Graz, A-8010 Graz, Austria
SOURCE: Biochemical Journal, (1987) Vol. 242, No. 1, pp. 27-32.
ISSN: 0264-6021 CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical and Experimental Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Dec 1991
Last Updated on STN: 11 Dec 1991

AB Reports of two independent studies suggest that familial hyperalphalipoproteinaemia (FHALP) may be caused by a deficiency of cholesteryl ester transferase/exchange activity (CETP). We also have studied CEPT in the plasma of an Italian FHALP kindred. The study group was divided into blood relatives with > 1.70 mM high-density-lipoprotein cholesterol (HLDL-C) (group I, n=9), with < 1.70 mM-HDLC-C (group II, n=12) and in spouses (group III, n=6). Two different assays were performed to measure CETP activity. In method A the interfering endogenous lipoproteins in the plasma samples were removed by poly(ethylene glycol) precipitation or by ultracentrifugation at a relative density (d) of 1.180. The CETP-activity of these samples was measured in a system consisting of fixed amounts of HDL and cholesteryl [1-(14)C]oleate-labelled low-density lipoproteins (LDL). In method B, trace amounts of HDL (radiolabelled with cholesteryl [1-(14)C]oleate) were incubated with plasma for 3 h at 37 ° C and the distribution of the label among lipoproteins was measured (CET activity). The results can be summarized as follows. The mean CETP activities measured by method A were 187, 213 and 243 nmol/h per ml in groups I, II and III respectively. The proband with the highest HDL-C (4.98 mM) had a CETP activity of 231 nmol/h per ml. The corresponding CET activities measured by method B and expressed as percentage transfer/h were 4.3, 8.0 and 11.2 in groups I-III. The proband with HDL-C = 4.98 mM had a value of only 1.7%/h. There was a strong negative correlation between percentage CE transfer and HDL-C concentration. Calculating these data in terms of CE exchange (nmol/h per ml), groups I, II and III exhibited mean activities of 86, 124 and 110 nmol/h per ml respectively; for the proband this value was 80 nmol/h per ml. Only a slight correlation was found between these values and the HDL-C value. Thus by both methods, (A), measuring the CETP activity per se and (B), measuring the activity in whole plasma (reflecting the activity of the protein and the concentration and composition of lipoproteins), no major differences could be found between the three groups.. In our family, therefore, no connection between FHALP and CETP deficiency could be found. It is concluded that, for hyper- and dys-lipoproteinaemic samples, a careful selection of the assay procedure

as well as the mode of calculating results is essential. Since this may not hold the previous studies, the supposed connection between FHALP and CETP deficiency is challenged.

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     (FILE 'HOME' ENTERED AT 14:21:30 ON 05 OCT 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:21:55 ON 05 OCT 2007
L1             0 S CHOLESTRYL (W)ESTER (W)TRANSFERASE?
L2            64 S ESTER (W)TRANSFERASE?
L3       8648767 S CLON? OR EXPRESS? OR RECOMBINANT
L4            15 S L2 AND L3
L5            12 DUP REM L4 (3 DUPLICATES REMOVED)

=> s "LIPAM-6"
L6             0 "LIPAM-6"

=> s lipid (w)associated
L7          2983 LIPID (W) ASSOCIATED

=> s l7 and transferase?
L8            24 L7 AND TRANSFERASE?

=> s l3 and l8
L9             1 L3 AND L8

=> d ibib ab

L9    ANSWER 1 OF 1  BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-07184  BIOTECHDS
TITLE:            Novel viral vector comprising beta-catenin/bipartite T-cell
                  factor-responsive promoter having first and second promoter
                  region linked to target nucleic acid sequence, useful for
                  treat- ing colon cancer;
                       recombinant virus vector for use in disease
                     therapy and gene therapy
AUTHOR:           HUNG M; KWONG K Y; ZOU Y
PATENT ASSIGNEE:  HUNG M; KWONG K Y; ZOU Y
PATENT INFO:      US 2003228285 11 Dec 2003
APPLICATION INFO: US 2003-429802 5 May 2003
PRIORITY INFO:    US 2003-429802 5 May 2003; US 2002-377672 3 May 2002
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2004-042209 [04]
AB    DERWENT ABSTRACT:
      NOVELTY - Viral vector (I) comprising beta-catenin/bipartite T-cell
      factor (Tcf)-responsive promoter construct which comprises a first
      promoter region having a copy of Tcf/LEF-1 binding site operatively
      linked to a second promoter region, and a nucleic acid sequence, where
      first and second promoter regions are operatively linked to target
      nucleic acid sequence, is new.
           DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
      following: (1) a nucleic acid segment (II) comprising
      beta-catenin/Tcf-responsive promoter construct comprising a first
      promoter region having a Tcf/LEF-1 binding site operatively linked to a
      second promoter being a minimal CMV promoter; and (2) screening (M1) for
      a modifier of beta-catenin activity involves providing a
      beta-catenin/Tcf-responsive promoter construct comprising a first
      promoter region having one or more copy of a Tcf/LEF-1 binding site,
      operatively linked to, a second promoter, and a reporter nucleic acid
      sequence, where the first and second promoter regions are operatively
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linked to the reporter nucleic acid sequence, introducing to the vector a test compound, and assaying for a change associated with the reporter nucleic acid sequence, where when change occurs, test compound is modified.

WIDER DISCLOSURE - The following are also disclosed: (1) purified proteins, polypeptides or peptides comprising beta-catenin/Tcf-responsive promoter; (2) composition comprising one or more lipids associated with (I); (3) identifying whether the activation of beta-catenin is altered, such as for identification of cancer cell to be treated; and (4) in vivo methods of imaging beta-catenin activation using antibody conjugates.

BIOTECHNOLOGY - Preferred Viral Vector: (I) is an adenoviral vector. In (I), the first promoter region is further defined as a minimal CMV promoter, TK promoter, fos promoter, or E2F promoter. The beta-catenin/Tcf-responsive promoter comprises three or more copies of a Tcf/LEF-1 binding site and the second promoter region comprises a minimal CMV promoter. (I) encodes TOP-CMV promoter. The nucleic acid sequence is a suicide nucleic acid sequence, a toxin nucleic acid sequence, a pro-apoptotic nucleic acid sequence, a cytokine nucleic acid sequence, an anti-angiogenic nucleic acid sequence, a cancer suppressor nucleic acid sequence, or a combination of these. The suicide nucleic acid sequence encodes thymidine kinase, cytosine deaminase, p450 oxidoreductase, carboxypeptidase G2, beta-glucuronidase, penicillin-V-amidase, penicillin-Gamidase, beta-lactamase, nitroreductase, carboxypeptidase A, linamarase, Escherichia coli gpt, or E.coli Deo. The nucleic acid sequence encodes a cancer suppressor nucleic acid sequence encoding p53 or Rb. A pro-apoptotic nucleic acid sequence, encodes p15, p16, or p21WAF-1. A cytokine nucleic acid sequence, encodes granulocyte macrophage colony stimulating factor, tumor necrosis factor alpha, interferon alpha, interferon gamma, IL1, IL2, IL3, IL4, IL6, IL7, IL10, IL12, or IL15. (I) is comprised in a pharmaceutical composition. Preferred Nucleic Acid: (II) further comprises a region encoding therapeutic polypeptide under the operative control of beta-catenin/Tcf-responsive promoter. (II) is comprised in non-viral vector such as plasmid or a liposome, a viral vector such as adenoviral, retroviral or an adeno-associated viral vector or in both. (II) is comprised in pharmaceutical composition. Preferred Method: In (M1), the assaying step involves detecting transcription rate or level of reporter nucleic acid sequence which decreases when the test compound is an inhibitor of beta-catenin activity. The reporter is green fluorescent protein, blue fluorescent protein, beta-galactosidase, chloramphenicol acetyl transferase, or luciferase. The test compounds is a small molecule, a polypeptide, polynucleotide, sugar, carbohydrate, lipid or a combination of these. (M1) occurs in a cell and further involves administering the inhibitor in a pharmaceutical composition to an individual having cancer related to a defective Wnt/beta-catenin pathway.

ACTIVITY - Cytostatic. No supporting data is given.

MECHANISM OF ACTION - Gene therapy; beta-catenin activity inhibitor.

USE - (I) is useful for treating an individual with colon cancer which is metastasized to the liver which involves administering (I) where the nucleic acid sequence encodes a therapeutic polypeptide or thymidine kinase, a prodrug and chemotherapy, radiation, surgery or gene therapy to the individual. The prodrug is ganciclovir, acyclovir, FIAU (1-(2-deoxy-2-fluoro-beta-D-arabinofuranosyl)-5-iodouracil), ifosfamide, 6-methoxypurine arabinoside, 5-fluorocytosine, doxorubicin, CB1954, nitrofurazone, N-(Cyanoacetyl)-L-phenylalanine, or N-(3-chloropropinoyl)-L-phenylalanine (claimed).

ADMINISTRATION - (I) is administered parenterally, orally, nasally, or topically at a dosage of 0.01-5.0 mg/kg body weight.

EXAMPLE - Multiple beta-catenin/bipartite T-cell factor (Tcf)-responsive promoters that can selectively target colon cancer were analyzed. The activities of five sets of beta-catenin/Tcf-responsive promoters were compared in colon cancer cell lines. Two well-characterized colon cancer cell lines SW480 and DLD-I, were

selected. In both of the cell lines the adenomatous polyposis coli (APC) gene was mutated and beta-catenin levels were evaluated. Chang liver and SK-HEP-1 cell lines were included in the study as controls. These two cell lines were derived from the origins and exhibited very low level of beta-catenin/Tcf transcription activity. The five promoters contained three copies of beta-catenin/Tcf-binding site sequences (wild-type beta-catenin/Tcf-binding sites in TOP promoter and mutated beta-catenin/Tcf-binding sites in FOP promoters). AT to GC changed in the FOP sequences abolished Tcf/LEF-1 binding and rendered the promoters non-responsive to beta-catenin. To construct beta-catenin/Tcf-responsive promoters, three copies of the Tcf/LEF-1 binding oligomers were fused with minimal promoters from viral origins (TOP-CMV, TOP-TK), human cellular genes (TOP-hTERT, TOP-fos), or a combination of human and viral promoter elements (TOP-E2F-CMV). A corresponding control plasmid was constructed for each promoter by replacing the TOP oligomers with the mutant Gcf binding oligomers FOP. TOP and FOP elements were generated by digestion of TOP-fos-LUC, FOP-fos-LUC, TOPTK-LUC, or FOPTK-LUC plasmids. The activities of the promoters were measured with luciferase assays. Transfection experiments were normalized by the Dual Luciferase system. Control plasmid RL-TK (0.2 mug) was used for normalization. Luciferase activities were measured 24-36 hours after transfection. Except for TOP-hTERT, all beta-catenin/Tcf-responsive promoters were selectively activated in colon cancer cell lines where the TOP/FOP ratios were much higher in the colon cancer cells (SW480 and DLD-1) than in liver-derived cells (Chang liver and SK-HEP-1). However, TOP-CMV exhibited much higher activity than any other beta-catenin/Tcf-responsive promoters in the two colon cancer cell lines. Because of its high selectivity and activity in the colon cancer cell lines, TOP-CMV promoter was utilized. (114 pages)

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:21:55 ON 05 OCT 2007
L1             0 S CHOLESTRYL (W)ESTER (W)TRANSFERASE?
L2            64 S ESTER (W)TRANSFERASE?
L3       8648767 S CLON? OR EXPRESS? OR RECOMBINANT
L4            15 S L2 AND L3
L5            12 DUP REM L4 (3 DUPLICATES REMOVED)
L6             0 S "LIPAM-6"
L7          2983 S LIPID (W)ASSOCIATED
L8            24 S L7 AND TRANSFERASE?
L9             1 S L3 AND L8

=> e saratoga x j/au
E1             5      SARATNIKOV A S/AU
E2             1      SARATO FUMIO/AU
E3             0 --> SARATOGA X J/AU
E4             1      SARATOGLU N/AU
E5             1      SARATOLEANU D/AU
E6             1      SARATORE F A/AU
E7             1      SARATOSIS P/AU
E8             5      SARATOV A D/AU
E9             1      SARATOV A F/AU
E10            2      SARATOV A I/AU
E11            1      SARATOV A S/AU
E12            1      SARATOV A YU/AU

=> e jian x/au
E1             1      JIAN WUDAI/AU
E2             1      JIAN WY/AU
E3           172 --> JIAN X/AU
```

```
E4              3      JIAN X A/AU
E5              1      JIAN X B/AU
E6             44      JIAN X C/AU
E7              5      JIAN X D/AU
E8              1      JIAN X E/AU
E9              5      JIAN X F/AU
E10           145      JIAN X G/AU
E11             8      JIAN X H/AU
E12             2      JIAN X J/AU

=> e jiang x/au
E1              4      JIANG WW/AU
E2              3      JIANG WZ/AU
E3           3488 --> JIANG X/AU
E4              4      JIANG X A/AU
E5              1      JIANG X A Y A/AU
E6             52      JIANG X B/AU
E7            354      JIANG X C/AU
E8            200      JIANG X D/AU
E9              4      JIANG X E/AU
E10           197      JIANG X F/AU
E11           183      JIANG X G/AU
E12           447      JIANG X H/AU

=> s e3
L10          3488 "JIANG X"/AU

=> e becha s d/au
E1             10      BECHA M B/AU
E2              8      BECHA S/AU
E3            124 --> BECHA S D/AU
E4              8      BECHA SHANYA/AU
E5            126      BECHA SHANYA D/AU
E6             12      BECHAC/AU
E7             68      BECHAC G/AU
E8             10      BECHAC J P/AU
E9              8      BECHADE A/AU
E10            80      BECHADE C/AU
E11            33      BECHADE CATHERINE/AU
E12           209      BECHADE D/AU

=> s e5
L11           126 "BECHA SHANYA D"/AU

=> e yang y g/au
E1            921      YANG Y F/AU
E2              1      YANG Y F D/AU
E3            458 --> YANG Y G/AU
E4           1915      YANG Y H/AU
E5              8      YANG Y H C/AU
E6              1      YANG Y H H/AU
E7             28      YANG Y H J/AU
E8             10      YANG Y H JOY/AU
E9             33      YANG Y H K/AU
E10             3      YANG Y H KAO/AU
E11             2      YANG Y H P/AU
E12             1      YANG Y H YONG HUA/AU

=> s e3
L12           458 "YANG Y G"/AU

=> e swarnaker a/au
E1             49      SWARNAKAR SNEHASIKTA/AU
E2             10      SWARNAKAR V/AU
```

```
E3              3 --> SWARNAKER A/AU
E4              3     SWARNAKER ANITA/AU
E5              1     SWARNAKER RAMDAYAL/AU
E6              1     SWARNAKER SNEHASIKTA/AU
E7              1     SWARNAKER V/AU
E8              3     SWARNAKUMAR K G/AU
E9              1     SWARNAKUMAR N S/AU
E10             1     SWARNAKUMARI C/AU
E11             2     SWARNAKUMARI G/AU
E12             2     SWARNAKUMARI V G/AU

=> s e4
L13             3 "SWARNAKER ANITA"/AU

=> e bulloch s a/au
E1              1     BULLOCH RON C/AU
E2              6     BULLOCH S/AU
E3             23 --> BULLOCH S A/AU
E4              3     BULLOCH SCOTT/AU
E5              4     BULLOCH SEAN/AU
E6             22     BULLOCH SEAN A/AU
E7              3     BULLOCH T/AU
E8              4     BULLOCH W/AU
E9              1     BULLOCH W C/AU
E10             7     BULLOCH WILLIAM/AU
E11             2     BULLOCH WM/AU
E12             3     BULLOCK/AU

=> s e3-e6
L14            52 ("BULLOCH S A"/AU OR "BULLOCH SCOTT"/AU OR "BULLOCH SEAN"/AU OR
                  "BULLOCH SEAN A"/AU)

=> d his

     (FILE 'HOME' ENTERED AT 14:21:30 ON 05 OCT 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:21:55 ON 05 OCT 2007
L1              0 S CHOLESTRYL (W)ESTER (W)TRANSFERASE?
L2             64 S ESTER (W)TRANSFERASE?
L3        8648767 S CLON? OR EXPRESS? OR RECOMBINANT
L4             15 S L2 AND L3
L5             12 DUP REM L4 (3 DUPLICATES REMOVED)
L6              0 S "LIPAM-6"
L7           2983 S LIPID (W)ASSOCIATED
L8             24 S L7 AND TRANSFERASE?
L9              1 S L3 AND L8
                  E SARATOGA X J/AU
                  E JIAN X/AU
                  E JIANG X/AU
L10          3488 S E3
                  E BECHA S D/AU
L11           126 S E5
                  E YANG Y G/AU
L12           458 S E3
                  E SWARNAKER A/AU
L13             3 S E4
                  E BULLOCH S A/AU
L14            52 S E3-E6

=> s l10 or l11 or l12 or l13 or l14
L15          4093 L10 OR L11 OR L12 OR L13 OR L14

=> s l2 and l15
```

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L16             0 L2 AND L15

=> s l8 and l15
L17             0 L8 AND L15

=> s l15 and transferase?
L18            24 L15 AND TRANSFERASE?

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19            17 DUP REM L18 (7 DUPLICATES REMOVED)

=> d 1-17 ibib ab

L19   ANSWER 1 OF 17  BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2007-17822  BIOTECHDS
TITLE:            Novel transgenic knockout animal, whose genome comprises a
                  heterozygous disruption of at least one endogenous gene
                  encoding a serine palmitoyl-CoA transferase
                  subunit, useful for studying a metabolic syndrome;
                  involving serine palmitoyl-CoA transferase gene
                  knockout in transgenic mouse useful for screening a drug
                  compound for treating arteriosclerosis and for studying
                  insulin resistance syndrome, obesity and diabetes
AUTHOR:           JIANG X; HOJJATI M R
PATENT ASSIGNEE:  JIANG X
PATENT INFO:      WO 2007030556 15 Mar 2007
APPLICATION INFO: WO 2006-US34743 7 Sep 2006
PRIORITY INFO:    US 2005-714876 7 Sep 2005; US 2005-714876 7 Sep 2005
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2007-458050 [44]
AB    DERWENT ABSTRACT:
      NOVELTY - A transgenic knockout animal e.g. mammal, for studying a
      metabolic syndrome or atherosclerosis, whose genome comprises a
      heterozygous disruption of at least one endogenous gene encoding a serine
      palmitoyl-CoA transferase (SPT) subunit, is new.
           DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the
      following: (1) screening drugs for treating atherosclerosis, involves
      obtaining or generating an animal model for atherosclerosis,
      administering test candidate molecules or compounds of specific
      ligands/inhibitors of Sptlc1 and/or Sptlc2 to the animal, and screening
      for the molecules or compounds that can treat atherosclerosis; (2) a
      ligand/inhibitor obtained by the screening method; and (3) preventing or
      treating atherosclerosis, involves administering a myriocin to a subject.
           BIOTECHNOLOGY - Preparation: The transgenic animal is generated by
      standard recombinant methods (disclosed). Preferred Transgenic Animal:
      The genome of the animal comprises a heterozygous disruption of SPtlc1 or
      Sptlc2. The animal is a mouse.
           ACTIVITY - Antiarteriosclerotic. Eight-week-old apoE knock out (KO)
      mice were administered either with myriocin (0.3 mg/kg) or phosphate
      buffered saline (control) for 8 weeks. The animals were fed with Purina
      Rodent Chow (catalog number 5001) or a high fat, high cholesterol diet
      (20% milk fat and 0.15% cholesterol). Plasma spingomyelin (SM),
      cholesterol and phosphatidylcholine (PC) levels were analyzed by fast
      protein liquid chromatography (FPLC). The results showed that myriocin
      treatment significantly decreased plasma SM levels and increased plasma
      PC levels but had no effect on plasma cholesterol levels in the mice on a
      chow diet or a high fat diet.
           MECHANISM OF ACTION - Serine palmitoyl-CoA transferase
      inhibitor.
           USE - For screening drugs for treating atherosclerosis or studying a
      metabolic syndrome such as insulin resistance syndrome, obesity or
      diabetes. The ligand/inhibitor is useful for preventing or treating
```

atherosclerosis (both claimed).

ADMINISTRATION - The myriocin is administered by intravenous, subcutaneous, intramuscular, or intraperitoneal route (claimed). No dosage details given.

ADVANTAGE - The transgenic animal enables to examine the phenotypic consequences resulting from heterozygous deficiency of the Sptlc1 or Sptlc2 gene.

EXAMPLE - About 12 kb mouse genomic DNA fragment, containing Sptlc1 exon 7-10 from the mouse 129 lambda genomic library, was utilized for targeting vector construction. Embryonic stem (ES) cells were electroporated by PacI-linearized targeting vector and screened by selection with G418. Southern blot analysis and PCR were used for screening the targeted ES cells. Genomic DNA was digested with ECoRV and a 350-bp DNA fragment, just 3' to the targeting vector, was used as a probe for Southern blots. The wild type (WT) contained a 7.2 kb fragment, while the recombinant contained a 5.5 kb fragment without exon 7 or 8. PCR was done using primer pairs SrSA5 and Neo2. The positive clones gave rise to a 1.0 kb PCR fragment. The correctly targeted ES cell lines were microinjected into C57BL/6J blastocysts. Chimeric mice were generated and provided germline transmission of the disrupted Sptlc1 gene. Chimeric males were mated with C57BL/6 females and the resulting F1 animals containing the disrupted allele were intercrossed to generate F2 mice. These were backcrossed with C57BL/6 mice for five generations. AU phenotypic characterizations were performed with wild-type (+/+) and heterozygous (plus minus) within the same generation, all animals 10 to 12 weeks old. To investigate whether a reduction of SPT activity had any impact on plasma sphingolipid levels, including sphingomyelin (SM), lysoSM, Cer, S1P and Sph, the mass spectrometer (MS) was utilized. The results showed that plasma Cer, S1P and Sph were significantly decreased in both Sptlc1 plus minus mice, compared with WT animals, while plasma total SM did not change.(65 pages)

L19 ANSWER 2 OF 17 EMBASE

ACCESSION NUMBER: 2007094947 EMBASE

TITLE: Lipid peroxidation and the protective effect of physical exercise on breast cancer.

AUTHOR: Gago-Dominguez M.; Jiang X.; Esteban Castelao J.

CORPORATE SOURCE: M. Gago-Dominguez, USC/Norris Comprehensive Cancer Center, Department of Preventive Medicine, Keck School of Medicine, Los Angeles, CA 90033-0800, United States. mgago@usc.edu

SOURCE: Medical Hypotheses, (2007) Vol. 68, No. 5, pp. 1138-1143.
Refs: 59
ISSN: 0306-9877 CODEN: MEHYDY

PUBLISHER IDENT.: S 0306-9877(06)00683-9

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
017 Public Health, Social Medicine and Epidemiology
029 Clinical and Experimental Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 28 Mar 2007
Last Updated on STN: 28 Mar 2007

AB Physical exercise has been found to decrease the risk of breast cancer by undefined means. In our prior communication, we proposed lipid peroxidation to be a relevant mechanism for breast cancer protection associated with many established protective factors such as parity, oophorectomy, menopause, physical exercise, etc. [Gago-Dominguez M, Castelao J, Pike MC, Sevanian A, Haile RW. Role of lipid peroxidation in the epidemiology and prevention of breast cancer. Cancer Epidemiol Biomark Prevent 2005;14:2829-39]. In the present communication, we examine in detail the physical exercise-breast cancer relationship in light of the lipid peroxidation mechanism. We provide additional

supporting evidence for the hypothesis that oxidative stress-induced apoptosis may be a mechanism responsible, at least in part, for the protective effect of exercise in breast cancer. Specifically, we describe (1) the sources of free radicals occurring during exercise, (2) existing experimental data on physical exercise, lipid peroxidation and cancer, (3) existing supporting data implicating exercise-induced reactive oxygen species (ROS) as the mechanism responsible for increased apoptosis in different cell systems, and (4) changes in the antioxidant enzymes glutathione S transferases (GSTs), superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase (CAT) that occur after physical exercise, which are believed to be a physiologic response to oxidative stress induced by physical exercise. .COPYRGT. 2006.

L19 ANSWER 3 OF 17 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007395010 EMBASE
TITLE: Studies on the metabolism of 4-methyl-piperazine-1-carbodithioc acid 3-cyano-3,3-diphenylpropyl ester hydrochloride in rats by high-performance liquid chromatography/electrospray ionization tandem mass spectrometry.
AUTHOR: Jiang X.; Ling X.; Han F.; Li R.; Cui J.
CORPORATE SOURCE: X. Ling, Department of Pharmaceutical Analysis, School of Pharmaceutical Sciences, Peking University, Xueyuan Road 38, Beijing, 100083, China. pkulxm@126.com
SOURCE: Journal of Pharmaceutical and Biomedical Analysis, (3 Sep 2007) Vol. 44, No. 5, pp. 1127-1132.
Refs: 15
ISSN: 0731-7085 CODEN: JPBADA
PUBLISHER IDENT.: S 0731-7085(07)00283-X
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 2007
Last Updated on STN: 4 Sep 2007

AB 4-Methyl-piperazine-1-carbodithioc acid 3-cyano-3,3-diphenylpropyl ester hydrochloride(TM208) is a newly synthesized compound, which has shown excellent in vivo and in vitro anticancer activity and low toxicity. In this study, the metabolism of TM208 in rats was studied for the first time by high-performance liquid chromatography coupled with tandem mass spectrometry. Following a single oral administration to rats, TM208 was metabolized to eight metabolites (M1-M8). M1 is the desmethyl metabolite and the acylation of M1 with N-acetyl transferase results in M6 (N-acetyl metabolite), M5 is N-formyl metabolite; M4 is phenyl monohydroxylation metabolite, M2 is the sulfine metabolite of TM208, and M3 is also an odd-oxygen added products which the possible oxidation site has described in this paper; M8 is the metabolite resulting from the replacement of '-C{double bond, long}S' with '-C{double bond, long}O', M7 is a ring-opened piperazine oxidation products to a kind of acid.

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ACCESSION NUMBER: 2006625234 EMBASE
TITLE: Aclarubicin-loaded cationic albumin-conjugated pegylated nanoparticle for glioma chemotherapy in rats.
AUTHOR: Lu W.; Wan J.; Zhang Q.; She Z.; Jiang X.
CORPORATE SOURCE: X. Jiang, Department of Pharmaceutics, School of Pharmacy, Fudan University (Fenglin Campus), 138 Yi Xue Yuan Road, Shanghai 200032, China. xgjiang@shmu.edu.cn
SOURCE: International Journal of Cancer, (15 Jan 2007) Vol. 120,

No. 2, pp. 420-431.
Refs: 56
ISSN: 0020-7136 E-ISSN: 1097-0215 CODEN: IJCNAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
039 Pharmacy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2007
Last Updated on STN: 31 Jan 2007

AB Traditional glioma chemotherapy with those second-line drugs such as anthracyclines usually failed because they are inaccessible to blood-brain barrier (BBB) in tumor. In our study, we incorporated aclarubicin (ACL) into cationic albumin-conjugated pegylated nanoparticle (CBSA-NP-ACL) to determine its therapeutic potential of rats with intracranially implanted C6 glioma cells. When labeled with fluorescent probe, 6-coumarin, CBSA-NP was shown to accumulate much more in tumor mass than nanoparticle without conjugated CBSA (NP) 1 hr post intravenous injection, as well as better retention after 24 hr. Tumor drug concentration of CBSA-NP-ACL displayed 2.6- and 3.3-fold higher than that of NP-ACL and ACL solution 1 hr post injection, while 2.7 and 6.6-fold higher after 24 hr, respectively. Moreover, using tumor microdialysis sampling, AUC(0-24 hr) of free drug amount in tumor interstitium delivered by CBSA-NP-ACL was about 2.0- and 2.7-fold higher than that of NP-ACL and ACL solutions, respectively. When the tumor rat model was subjected to 4 cycles of 2 mg/kg of ACL in different formulations, a significant increase of median survival time was found in the group of CBSA-NP-ACL compared with that of saline control animals, animals treated with NP-ACL and ACL solution. By terminal deoxynucleotitlyl transferase-mediated dUTP nick-end-labeling, CBSA-NP-ACL can extensively make the tumor cell apoptosis. Histochcmical evaluation by periodic acid Shiff staining and biochemical analysis depicted that the incorporation of ACL into CBSA-NP reduced its toxicity to liver, kidney and heart. Besides, CBSA-NP-ACL was not shown to open tight junction evaluated by BBB coculture. It was concluded that CBSA-NP-ACL could have a therapeutic potential for treatment of glioma.

L19 ANSWER 5 OF 17 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2007297300 EMBASE
TITLE: Tolerance in xenotransplantation.
AUTHOR: Yang Y.-G.; Sykes M.
CORPORATE SOURCE: Dr. M. Sykes, Transplantation Biology Research Center, Massachusetts General Hospital/Harvard Medical School, MGH-East Building 149-5102, 13th Street, Boston, MA 02129, United States. megan.sykes@tbrc.mgh.harvard.edu
SOURCE: Current Opinion in Organ Transplantation, (Apr 2007) Vol. 12, No. 2, pp. 169-175.
Refs: 27
ISSN: 1087-2418 E-ISSN: 1531-7013 CODEN: COOTAB
PUBLISHER IDENT.: 00075200200704000000012
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB PURPOSE OF REVIEW: This review assesses recent progress in the induction of xenograft tolerance, with a focus on the strategies showing promise in preclinical large animal models. RECENT FINDINGS: True xenograft tolerance has been limited to rodent models. In large animal models, T

cell costimulatory blockers have been widely used as a key component of immunosuppression in controlling xenograft rejection. Despite significant improvements in xenograft survival, blocking T cell costimulation has not yet shown the ability to achieve tolerance in primates. Development of an effective, nontoxic recipient conditioning regimen allowing donor marrow cell engraftment will be essential to the translation of the mixed chimerism approach to clinical xenotransplantation. Costimulatory blockade has been shown to promote this type of tolerance in rodent xenograft models. Thymic xenotransplantation with Gal-transferase knockout source pigs, for the first time, permitted porcine kidney xenograft survival in nonhuman primates for several months without rejection. SUMMARY: Tolerance induction is likely to be critical for clinical success of xenotransplantation. With further investigation, induction of xenotransplantation tolerance may be achieved in nonhuman primates and ultimately in humans.

L19 ANSWER 6 OF 17 EMBASE

ACCESSION NUMBER: 2006325551 EMBASE

TITLE: Expression of tumor necrosis factor α and neuronal apoptosis in the developing rat brain after neonatal stroke.

AUTHOR: Mao M.; Hua Y.; Jiang X.; Li L.; Zhang L.; Mu D.

CORPORATE SOURCE: D. Mu, Department of Pediatrics, West China Second University Hospital, Sichuan University, Chengdu, Sichuan 610041, China. dezhi.mu@ucsf.edu

SOURCE: Neuroscience Letters, (7 Aug 2006) Vol. 403, No. 3, pp. 227-232.
Refs: 22
ISSN: 0304-3940 CODEN: NELED5

PUBLISHER IDENT.: S 0304-3940(06)00259-X

COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 25 Jul 2006
Last Updated on STN: 25 Jul 2006

AB Increased expression of tumor necrosis factor α (TNFα) has been shown in adult stroke models. However, its expression and relationship with neuronal apoptosis in neonatal rats with transient middle cerebral artery occlusion (MCAO) have not been clearly elucidated. We studied the expression and distribution of TNFα and neuronal apoptosis in a postnatal Day 10 rat MCAO model using reverse transcriptase-polymerase chain reaction (RT-PCR), Western blot, immunohistochemistry, fluorescence double-labeling, and terminal deoxynucleotidyl transferase biotin-dUTP nick end labeling (TUNEL) analyses. We found TNFα mRNA expression increased at 2 h and was maintained at high levels until 24 h after reperfusion. TNFα protein expression was significantly increased from 4 to 8 h ($p < 0.01$) lasting through 24 h ($p < 0.05$) after reperfusion compared to the sham controls. TNFα immunoreactive cells were colocalized to neurons in both the core and the penumbra areas of the ischemic cortex. However, apoptotic cells were mainly distributed in the penumbra area and colocalized to neurons as well as to TNFα immunoreactive cells in the ischemic cortex. Our findings suggest that TNFα expression increases after neonatal stroke and is associated with neuronal apoptosis after transient focal cerebral ischemia.

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ACCESSION NUMBER: 2007024460 EMBASE

TITLE: Association between partial indexes of angiotensinogen gene polymorphisms and the risk of essential hypertension: A community case-control study.

AUTHOR: Zhan Y.-Y.; Jiang X.; Sheng H.-H.; Lin G.; Li J.; Cheng Y.-L.; Huang J.

CORPORATE SOURCE: Prof. Y.-Y. Zhan, Department of Cardiology, Nanjing Medical University, Nanjing 210029 Jiangsu Province, China

SOURCE: Chinese Journal of Clinical Rehabilitation, (Dec 2006) Vol. 10, No. 48, pp. 208-212.
Refs: 16
ISSN: 1671-5926 CODEN: ZLKHAH

COUNTRY: China

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
005 General Pathology and Pathological Anatomy

LANGUAGE: English

SUMMARY LANGUAGE: English; Chinese

ENTRY DATE: Entered STN: 23 Feb 2007
Last Updated on STN: 23 Feb 2007

AB Background: Angiotensinogen (AGT) gene is the firstly discovered candidate gene for essential hypertension, both the T174M and M235T polymorphisms locate at the second exons of AGT gene, and there is existence of linkage disequilibrium. The polymorphism at A-6G and G-217A sites in promotor region plays an important role in regulating the gene expression, and the products of keep close correlation with the level of blood pressure. Objective: To investigate the association between the polymorphism of AGT gene at A-6G, T174M and G-217A sites and the risk for the attack of essential hypertension in Chinese Han population. Design: A cluster sampling and case-control analysis. Settings: Department of Geriatrics and Department of Cardiology, the First Affiliated Hospital of Nanjing Medical University; Southern Research Center of National Human genome; Department of Cardiology, Dongtai People's Hospital of Jiangsu Province. Participants: The experiment was carried out in the countryside of Dongtai county, Yancheng city, Jiangsu province. All the subjects were selected from the countryside of Dongtai county, Yancheng city, Jiangsu province. Totally 177 patients with essential hypertension who had never accepted any drug treatment, were taken as the essential hypertension group, and hypertension was diagnosed according to the diagnostic standard of hypertension set by WHO/ISH in 1999 (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg); Another 86 normal person were taken as the normal control group. 2 Inclusive criteria: The enrolled subjects should be Han nationality; long-term local residents but not from other places; able to answer questions clearly; diagnosed by disease history, clinical symptoms, physical signs and assistant examinations; have complete data of investigation of uniform questionnaires by face-to-face interview (including demographic information, profession history, family history and life styles of smoking, drinking, drinking tea, etc.). 3 Exclusive criteria: The patients with secondary hypertension in the essential hypertension group, subjects having family history of hypertension in the normal control group, and those with chronic diseases of liver and kidney, and diabetes mellitus in both groups were excluded. Methods: Peripheral venous blood samples (3 mL) were collected, and DNA was extracted from human peripheral blood with FlexiGene DNA Kit (250). The Primer3 software was applied to design primers, and the polymorphism sites in the primer sequence were excluded. After multiplex polymerase chain reaction (PCR), 3 μL products were selected to detected the amplified results by agarose gel electrophoresis. The successfully amplified PCR products were purified with the QIAquick PCR Purification Kit, and the purified products were fragmentized with DNase I. The fragmentized products of enzyme digestion were labeled with

fluorescein by deoxynucleotide terminal transferase. Two allele specific probes and one mismatched probe were designed respectively for each single nucleotide polymorphism. The chips were prepared with the OmniGridTM 100 TLC sampler, each probe was repeated for three times to form three matrix. The hybridization solution was degenerated at 95 °C for 10 minutes, and then immediately cut on ice. 10 μL hybridization solution was added onto the chip matrix, hybridized at 50 °C for 2 hours, then washed and dried. The chips were scanned with the GenePix 4000B laser confocal scanner (Figure 2), and the intensity of the fluorescent signal for each probe was extracted with GenePix Pro, and the allele score of each single nucleotide polymorphism was calculated to judge the genotype. Main outcome measures: 1 Comparison of the frequencies of genotype distribution at each polymorphism site of AGT gene in both groups; 2 Correlation analysis of the polymorphism of AGT gene at A-6G and T-174M sites with the risk for the attack of essential hypertension; 3 Effects of the polymorphism of AGT gene at A-6G, T-174M and G-217A sites on blood pressure. Results: According to the intention-to-treat analysis, all the 263 subjects were involved in the analysis of results. 1 At the A-6G site of AGT gene, the frequencies of AA, AG and GG genotypes (P=0.014) and A and G alleles (P=0.004, OR=0.44) had significant differences between the essential hypertension group and normal control group; At the T174M site, the frequencies of CC, CT and TT genotypes (P=0.031) and A and G alleles (P=0.014, OR=0.55) were significantly different; At the G-217A site, no obvious differences were found in the GG, AG and AA genotypes (P=0.722) and G and A alleles (P=0.403, OR=0.80). 2 The risk of essential hypertension in the individuals carrying AA genotype of A-6G polymorphism and CC genotype of T174M polymorphism was reduced by 57% (95%CI= 0.23-0.82, P= 0.010) and 56% (95%CI= 0.25-0.79, P= 0.006) respectively. 3 There were no significant differences in the systolic blood pressure, diastolic blood pressure and mean arterial pressure among different genotypes at the A-6G, T174M sites and G-217A sites (F=0.100-2.911, P > 0.05). Conclusion: The AA genotype at A-6G and the CC genotype at T174M site of AGT gene may reduce the risk for the attack of essential hypertension in Chinese Han population, and no significant correlation was found between the type of G-217A polymorphism and the attack of essential hypertension.

L19 ANSWER 8 OF 17 EMBASE

ACCESSION NUMBER: 2005517328 EMBASE
TITLE: Design and characterization of viral polypeptide inhibitors targeting Newcastle disease virus fusion.
AUTHOR: Zhu J.; Jiang X.; Liu Y.; Tien P.; Gao G.F.
CORPORATE SOURCE: P. Tien, Center for Molecular Virology, Institute of Microbiology, Chinese Academy of Sciences, Zhongguancun Beiyitiao, Beijing 100080, China. tienpo@sun.im.ac.cn
SOURCE: Journal of Molecular Biology, (2 Dec 2005) Vol. 354, No. 3, pp. 601-613.
Refs: 33
ISSN: 0022-2836 CODEN: JMOBAK
PUBLISHER IDENT.: S 0022-2836(05)01151-4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
039 Pharmacy
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Dec 2005
Last Updated on STN: 8 Dec 2005

AB Paramyxovirus infections can be detected worldwide with some emerging zoonotic viruses and currently there are no specific therapeutic

treatments or vaccines available for many of these diseases. Recent studies have demonstrated that peptides derived from the two heptad repeat regions (HR1 and HR2) of paramyxovirus fusion proteins could be used as inhibitors of virus fusion. The mechanism underlying this activity is in accordance with that of class I virus fusion proteins, of which human immunodeficiency virus (HIV) and influenza virus fusion proteins are members. For class I virus fusion proteins, the HR1 fragment binds to HR2 to form a six-helix bundle with three HR1 fragments forming the central coiled bundle surrounded by three coiled HR2 fragments in the post fusion conformational state (fusion core). It is hypothesized that the introduced exogenous HR1 or HR2 can compete against their endogenous counterparts, which results in fusion inhibition. Using Newcastle disease virus (NDV) as a model, we designed several protein inhibitors, denoted HR212 as well asHR121 and 5-Helix, which could bind the HR1 or HR2 region of fusion protein, respectively. All the proteins were expressed and purified using a GST-fusion expression system in Escherichia coli. The HR212 or GST-HR212 protein, which binds the HR1 peptide in vitro, displayed inhibitory activity against NDV-mediated cell fusion, while the HR121 and 5-Helix proteins, which bind the HR2 peptide in vitro, inhibited virus fusion from the avirulent NDV strain when added before the cleavage of the fusion protein. These results showed that the designed HR212, HR121 or 5-Helix protein could serve as specific antiviral agents. These data provide additional insight into the difference between the virulent and avirulent strains of NDV.

L19 ANSWER 9 OF 17 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005054804 EMBASE
TITLE: NS-7, a novel Na(+)/Ca(2+) channel blocker, prevents neurologic injury after spinal cord ischemia in rabbits.
AUTHOR: Shi E.; Kazui T.; Jiang X.; Washiyama N.; Suzuki K.; Yamashita K.; Terada H.
CORPORATE SOURCE: Dr. T. Kazui, First Department of Surgery, Hamamatsu Univ. School of Medicine, Hamamatsu, Japan. tkazui@hama-med.ac.jp
SOURCE: Journal of Thoracic and Cardiovascular Surgery, (Feb 2005) Vol. 129, No. 2, pp. 364-371.
Refs: 30
ISSN: 0022-5223 CODEN: JTCSAQ
PUBLISHER IDENT.: S 0022-5223(04)00764-0
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Feb 2005
Last Updated on STN: 18 Feb 2005

AB Objective We investigated the neuroprotective effect of NS-7 (4-[4-fluorophenyl]-2-methyl-6- [5-piperidinopntyloxy] pyrimidine hydrochloride), a novel Na(+)/Ca(2+) channel blocker, on transient spinal cord ischemia in rabbits. Methods Spinal cord ischemia was induced in New Zealand white rabbits by means of infrarenal aortic occlusion for 20 minutes. Four experimental groups were enrolled. A sham group (n = 3) underwent the same operation without aortic occlusion. A control group (n = 7) received only saline before occlusion. Group A (n = 8) received NS-7 (1 mg/kg) 15 minutes before ischemia, and group B (n = 8) received NS-7 (1 mg/kg) at the onset of reperfusion. Neurologic function was assessed 24 and 48 hours after the operation with modified Tarlov criteria. Spinal cords were harvested for histopathologic examination and in situ terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL staining). Spinal cord infarction was investigated with 2, 3, 5-triphenyltetrazonlium chloride staining. Results Tarlov scoring demonstrated marked improvement in both group A and group B compared with

the control group at 24 and 48 hours after the operation. Minimal histologic changes were found in lumbar spinal cords of the 2 NS-7-treated groups, whereas severe neuronal necrosis was shown in the control group. TUNEL-positive neurons and the infarct size of lumbar spinal cords were significantly reduced by NS-7 administered both before ischemia and at the onset of reperfusion. No significant difference was noted between group A and group B in terms of spinal cord protection. Conclusion These results indicate that NS-7 protects the spinal cord against ischemic injury by preventing both neuronal necrosis and apoptosis. Copyright .COPYRGT. 2005 by The American Association for Thoracic Surgery.

L19 ANSWER 10 OF 17 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-27539 BIOTECHDS
TITLE: New oligonucleotide protein and antibody arrays of short-lived proteins are useful to compare expression levels of short-lived proteins under normal and diseased states and to screen for compounds that bind short-lived proteins; DNA array, protein array or antibody array for short-lived protein analysis
AUTHOR: LI X; JIANG X
PATENT ASSIGNEE: LI X; JIANG X
PATENT INFO: US 2003157540 21 Aug 2003
APPLICATION INFO: US 2003-347160 16 Jan 2003
PRIORITY INFO: US 2003-347160 16 Jan 2003; US 2002-53230 16 Jan 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-787334 [74]
AB DERWENT ABSTRACT:
NOVELTY - Arrays of short-lived proteins, oligonucleotides encoding short-lived proteins or antibodies against the short-lived proteins immobilized on a surface positioned in different defined regions are new.

DETAILED DESCRIPTION - (1) A new oligonucleotide array comprises a number of oligonucleotide probes immobilized on the surface of a substrate positioned in different defined regions on the surface, each probe comprising a binding region complementary to a portion of a different gene encoding a short-lived protein having a half life of less than 24 hours in its native cellular environment; (2) A new protein array comprises a number of short-lived proteins immobilized on a surface of a substrate positioned in different defined regions on the surface, where each protein has a half life of less than 24 hours in its native cellular environment; (3) A new antibody array comprising antibodies against short-lived proteins on the surface of a substrate positioned in different defined regions on the surface, where each protein has a half life of less than 24 hours in its native cellular environment

BIOTECHNOLOGY - Preferred Arrays: The short-lived protein preferably has a half life of less than 12 hours, most preferably less than 2 hours in it's native cellular environment. In the oligonucleotide array the probes are RNA, DNA or peptide nucleic acid (PNA), more preferably the DNA sequence of a portion of the cDNA of the short-lived protein or the DNA sequence of a portion of the 3' end of the sense strand of the gene encoding the protein. The probe is 20-100, more preferably 55-75 nucleotides and labeled with a detectable marker, preferably biotin, a radioisotope or a fluorescent marker. The density of the oligonucleotide array is between 100 and 1000000 and the diversity between 100-2000. In the protein array the portion of the full length protein is spotted on the array covalently or non-covalently and may be fused to a non-sort-lived protein, particularly a glutathione-S-transferase (claimed).

USE - The oligonucleotide array is used to determine expression levels of the short-lived proteins, particularly to compare expression levels in cells under normal and diseased states. The protein array is used to screen for agents that bind to the short-lived proteins, particularly cellular proteins contained in cell lysates. The antibody array is used to screen for short-lived proteins that bind to the

antibodies (claimed).

EXAMPLE - A membrane-based array of human SH3 sub-domains was constructed and screened for ligand-SH3 domain-specific interactions. Each SH3 domain binds to a conserved proline-rich motif on its ligand to initiate a protein interaction network. 38 recombinant glutathione-S-transferase (GST)-SH3 fusions were produced and spotted onto membranes. The binding site for SH3 domains from P13 kinase was detected with an antibody against the his tag of a P13-His fusion protein. Interaction was consistent with the published literature.(30 pages)

L19 ANSWER 11 OF 17 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 1

ACCESSION NUMBER: 2002217458 EMBASE
TITLE: Norwalk Virus binds to histo-blood group antigens present on gastroduodenal epithelial cells of secretor individuals.
AUTHOR: Marionneau S.; Ruvoen N.; Le MoullacVaidye B.; Clement M.; CailleauThomas A.; RuizPalacois G.; Huang P.; Jiang X.; Le Pendu J.
CORPORATE SOURCE: J. Le Pendu, INSERM U419, Institut de Biologie, 9 Quai Moncousu, 44093 Nantes Cedex 1, France.
jlependu@nantes.inserm.fr
SOURCE: Gastroenterology, (2002) Vol. 122, No. 7, pp. 1967-1977.
Refs: 45
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
048 Gastroenterology
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jul 2002
Last Updated on STN: 8 Jul 2002

AB Background & Aims: Norwalk Virus (NV) is a member of the Caliciviridae family, which causes acute epidemic gastroenteritis in humans of all ages and its cellular receptors have not yet been characterized. Another calicivirus, Rabbit Hemorrhagic Disease Virus, attaches to H type 2 histo-blood group oligosaccharide present on rabbit epithelial cells. Our aim was to test if, by analogy, recombinant NV-like particles (rNV VLPs) use carbohydrates present on human gastroduodenal epithelial cells as ligands. Methods: Attachment of rNV VLPs was tested on tissue sections of the gastroduodenal junction and on saliva from individuals of known ABO, Lewis, and secretor phenotypes. It was also tested on human Caco-2 cells and on animal cell lines transfected with glycosyl-transferases complementary DNA (cDNA). Competition experiments were performed with synthetic oligosaccharides and anticarbohydrate antibodies. Internalization was monitored by confocal microscopy. Results: Attachment of rNV VLPs to surface epithelial cells of the gastroduodenal junction as well as to saliva was detected, yet only from secretor donors. It was abolished by α1,2fucosidase treatment, and by competition with the H types 1 and 3 trisaccharides or with anti-H type I and anti-H types 3/4 antibodies. Transfection of CHO and TS/A cells with an α1,2fucosyltransferase cDNA allowed attachment of VLPs. These transfectants as well as differentiated Caco-2 cells expressing H type 1 structures internalized the bound particles. Conclusions: rNV VLPs use H type 1 and/or H types 3/4 as ligands on gastroduodenal epithelial cells of secretor individuals.

L19 ANSWER 12 OF 17 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-05392 BIOTECHDS
TITLE: Treating an individual, particularly bacterial diseases, e.g. otitis media, pneumonia, bacteremia, or meningitis, comprises

administering a modulator MurA polypeptides or enolpyruvyl transferases;
for use in otitis media, pneumonia, bacteremia, or meningitis infection therapy

AUTHOR: DU W; HUANG J; JIANG X; KALLENDER H; MCCLOSKEY L M; PAYNE D; REED S L; RITTENHOUSE S F; VAN HORN S; WALLIS N G
PATENT ASSIGNEE: SMITHKLINE BEECHAM CORP; SMITHKLINE BEECHAM PLC
PATENT INFO: WO 2001089303 29 Nov 2001
APPLICATION INFO: WO 2000-US14079 22 May 2000
PRIORITY INFO: WO 2000-14079 22 May 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-114258 [15]

AB DERWENT ABSTRACT:

NOVELTY - Treating an individual having need to inhibit MurA polypeptide or infected with a bacterium comprise administering a modulator of the UDP-N-acetylglucosamine enolpyruvyl transferase (MurA) or enolpyruvylshikimate-3-phosphate synthase (EPSPS), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) treating an individual having need to inhibit MurA polypeptide comprising administering to the individual an antibacterial amount of a compound or composition that inhibits or activates: (i) inhibition of EPSPS or MurA by aurin tricarboxylic acid; (ii) interaction between positively charged active site residues and an anionic tricarboxylate; or (iii) inhibition of MurA by rosolic acid; (2) treating an individual infected with a bacterium by administering to the individual a antibacterial amount of a compound or composition that inhibits or activates (i)-(iii) cited above; (3) treating an individual having need to inhibit MurA polypeptide or infected with a bacteria comprising administering to the individual a antibacterial compound or composition that inhibits an activity of a polypeptide consisting of an amino acid sequence that is at least 40-90% identical to a sequence having 419 amino acids fully defined in the specification or a sequence that is not defined in the specification, where the activity is (i)-(iii) cited above; (4) inhibiting a MurA polypeptide comprising contacting a compound or composition comprising the polypeptide with a compound or composition that inhibits or activates (i)-(iii) cited above; and (5) inhibiting or activating (i)-(iii) cited above, comprising contacting a compound or composition having bacteria with a compound or composition that inhibits or activates and activity of (i)-(iii) above to cause killing or slowing of growth of the bacteria.

ACTIVITY - Antibacterial; anti-inflammatory. No details of relevant tests given.

MECHANISM OF ACTION - Enolpyruvyl transferase modulator.

USE - The method is useful for modulating the activity of MurA polypeptides, particularly for treating microbial or bacterial diseases, e.g. otitis media, pneumonia, bacteremia, or meningitis.

ADMINISTRATION - None given. (49 pages)

L19 ANSWER 13 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2003088808 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12600088
TITLE: Expression of apoptosis of the skin lesion and muscle from patients with dermatomyositis.
AUTHOR: Zhang Y; Wang L; Jiang X; Zhang M; Cheng N
CORPORATE SOURCE: Department of Dermatovenereology, First Affiliated Hospital, WCUMS, Chengdu 610041, China.
SOURCE: Hua xi yi ke da xue xue bao = Journal of West China University of Medical Sciences = Huaxi yike daxue xuebao / [bian ji zhe, Hua xi yi ke da xue xue bao bian wei hui], (2001 Jun) Vol. 32, No. 2, pp. 213-5.
Journal code: 8609552. ISSN: 0257-7712.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 26 Feb 2003
Last Updated on STN: 19 Jun 2003
Entered Medline: 18 Jun 2003

AB OBJECTIVE: This study inquired into the relationship between the influence of corticosteroid and the expression of apoptosis, Fas and Bcl-2 in muscle from patients with dermatomyositis (DM). METHODS: Corticosteroid was given to group A (10 DM cases) but not given to group B (12 DM cases). RESULTS: Apoptotic cells were detected in situ by terminal deoxynucleotidyl transferase-mediated-dUTP nick end labeling (TUNEL). Fas and Bcl-2 expressions was determined with the use of immunohistochemical staining in DM. The results showed that more expression of apoptosis in keratinocytes, muscle cells and lymphocytes were observed in group A. The apoptotic index (AI) of muscle cells and that of lymphocytes were more marked in group A than in group B ($P < 0.05$). Less apoptosis cells were observed in two weeks of treatment, and no correlation was found between apoptosis and the lesion of skin and muscle. CONCLUSION: The authors suggest that corticosteroid may play a role in inducing the apoptosis of keratinocytes, muscle cells and lymphocytes, which may be one of the therapeutic mechanisms of corticosteroid. The length of administering corticosteroid to the patient's seems related to apoptosis.

L19 ANSWER 14 OF 17 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001103168 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11110984
TITLE: ABO genotyping by PCR-direct sequencing method.
AUTHOR: Jiang X; Hou G; Yu J; Huang B; Xu D
CORPORATE SOURCE: Liaoning Province Criminal Science and Technology Institute, Shenyang, Liaoning, 110032 P.R.China.
SOURCE: Zhonghua yi xue yi chuan xue za zhi = Zhonghua yixue yichuanxue zazhi = Chinese journal of medical genetics, (2000 Dec) Vol. 17, No. 6, pp. 432-5.
Journal code: 9425197. ISSN: 1003-9406.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 26 Jan 2001

AB OBJECTIVE: To analyze the sequence difference between human A, B, and O alleles and establish the method of ABO genotyping by PCR direct sequencing. METHODS: PCR-direct sequencing technique was used to analyze two regions of cDNA from A transferase gene, 233-433 and 660-788. RESULTS: Two nucleotide substitutions at 258th and 297th were found in 233-433 region, and a nucleotide substitution at 700th was found in 660-788 region. At 258th, the nucleotide was guanine in A and B alleles, and adenine in O allele. At 297th, the nucleotide was adenine in A allele, and guanine in B allele. As this position, O allele was subdivided into two types, O(A) and O(G). At 700th, the nucleotide was guanine in A and O alleles, and adenine in B allele. Therefore, 8 genotypes, AA, AO(A), AB, BB, BO(G), O(A) O(A), O(G) O(G) and O(A) O(G), could be clearly determined by only analyzing the 233-433 region. The other two genotypes, AO(G) and BO(A), could be further distinguished by analyzing the 660-788 region. CONCLUSION: The technique of PCR-direct sequencing provides an effective and new method for ABO genotyping further.

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ACCESSION NUMBER: 1999092211 EMBASE
TITLE: Hyperthermia-induced apoptosis and the inhibition of DNA laddering by zinc supplementation and withdrawal of calcium and magnesium in suspension culture of tobacco cells.
AUTHOR: Chen H.; Yan C.; Jiang X.; Dai Y.-R.
CORPORATE SOURCE: Y.-R. Dai, Department of Biology, Tsinghua University, Beijing 100084, China. zhaizhh@mail.tsinghua.edu.cn
SOURCE: Cellular and Molecular Life Sciences, (1999) Vol. 55, No. 2, pp. 303-309.
Refs: 24
ISSN: 1420-682X CODEN: CMLSFI
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Mar 1999
Last Updated on STN: 26 Mar 1999

AB In the present paper we report examination of stereotypic hallmarks of apoptosis in heat-treated tobacco cells. Hyperthermia (44°C, 4 h) caused apoptosis in 53.6% of cells when assayed 24 h after heat treatment. The induction of apoptosis by heat treatment was confirmed by flow cytometric assay. Cytological observations revealed condensation of the cytoplasm and nucleus, as well as nuclear collapse. DNA ladders were observed in DNA extracted from heat-treated cells, whereas DNA from control cells remained undegraded. The terminal deoxynucleotidyl transferase (TdT)-mediated dUTP nick end labeling (TUNEL) assay revealed that 51.8% of the heat-treated cells (44°C, 4 h) show positive reaction after a 24-h recovery. When cells were cultured in a medium supplemented with 0.4-5.0 mM ZnSO(4), internucleosomal DNA fragmentation induced by heat shock was completely negated. Strikingly, when cells were cultured in Ca(2+) and/or Mg(2+) free medium for 44 h followed by heat treatment, DNA laddering was not observed. The results suggest hyperthermia-induced apoptosis and a correlation between the regulation of endonucleases and heat shock signal in apoptotic tobacco cells.

L19 ANSWER 16 OF 17 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 1998377850 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9714048
TITLE: Mutation of galactose-1-phosphate uridyl transferase and its association with ovarian cancer and endometriosis.
AUTHOR: Morland S J; Jiang X; Hitchcock A; Thomas E J; Campbell I G
CORPORATE SOURCE: Obstetrics and Gynaecology, University of Southampton, Princess Anne Hospital, UK.
SOURCE: International journal of cancer. Journal international du cancer, (1998 Sep 11) Vol. 77, No. 6, pp. 825-7.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 25 Sep 1998
Last Updated on STN: 25 Sep 1998
Entered Medline: 14 Sep 1998

AB Impaired galactose metabolism has been proposed as a risk factor for ovarian cancer and endometriosis, which is a putative precursor of

endometrioid and clear cell histological sub-types of ovarian cancer. The prevalence of the most common galactose-I-phosphate uridyl transferase gene mutations, Q188R and N314D, was assessed in 206 women with ovarian cancer, 78 women with endometriosis and 248 controls. No Q188R mutations were found in any of the groups. A statistically significant increase in the frequency of N314D mutations was observed in women with serous and undifferentiated histological sub-types of ovarian cancer, but not mucinous, endometrioid or clear cell sub-types. There were no significant differences observed in the N314D mutation frequency between women with endometriosis (18%) and controls (17%). Our results support previous reports of an association of impaired galactose metabolism with serous and undifferentiated ovarian cancers but contradict previous findings of increased N314D mutation frequencies among women with endometriosis and endometrioid and clear cell sub-types ovarian cancer.

L19 ANSWER 17 OF 17 EMBASE

ACCESSION NUMBER: 1996070916 EMBASE
TITLE: Regulation of phospholipase D by protein kinase C is synergistic with ADP- ribosylation factor and independent of protein kinase activity.
AUTHOR: Singer W.D.; Brown H.A.; Jiang X.; Sternweis P.C.
CORPORATE SOURCE: P.C. Sternweis, Dept. of Pharmacology, Southwestern Medical Center, University of Texas, 5323 Harry Hines Blvd., Dallas, TX 75235-9041, United States
SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 8, pp. 4504-4510.
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Mar 1996
Last Updated on STN: 19 Mar 1996

AB Phospholipase D (PLD) which was partially purified from membranes of porcine brain could be stimulated by multiple cytosolic components; these included ADP-ribosylation factor (Arf) and RhoA, which required guanine nucleotides for activity, and an unidentified factor which activated the enzyme in a nucleotide-independent manner (Singer, W. D., Brown, H. A., Bokoch, G. M., and Sternweis, P. C. (1995) J. Biol. Chemical 270, 1494414950). Here, we report purification of the latter factor, its identification as the α isoform of protein kinase C (PKCα), and characterization of its regulation of PLD activity. Stimulation of PLD by purified PKCα or recombinant PKCα (rPKCα) occurred in the absence of any nucleotide and required activators such as Ca(2+) or phorbol ester. This action was synergistic with stimulation of PLD evoked by either Arf or RhoA. Dephosphorylation of rPKCα with protein phosphatase 1 or 2A resulted in a loss of its kinase activity, but had little effect on its ability to stimulate PLD either alone or in conjunction with Arf. Staurosporine inhibited the kinase activity of PKCα without affecting activation of PLD. Finally, gel filtration of PKCα that had been cleaved with trypsin demonstrated that stimulatory activity for PLD coeluted with the regulatory domain of the enzyme. These data indicate that PKC may regulate signaling events through direct molecular interaction with downstream effectors as well as through its well characterized catalytic modification of proteins by phosphorylation.

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(FILE 'HOME' ENTERED AT 14:21:30 ON 05 OCT 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 14:21:55 ON 05 OCT 2007

L1	0	S	CHOLESTRYL (W)ESTER (W)TRANSFERASE?
L2	64	S	ESTER (W)TRANSFERASE?
L3	8648767	S	CLON? OR EXPRESS? OR RECOMBINANT
L4	15	S	L2 AND L3
L5	12	DUP REM	L4 (3 DUPLICATES REMOVED)
L6	0	S	"LIPAM-6"
L7	2983	S	LIPID (W)ASSOCIATED
L8	24	S	L7 AND TRANSFERASE?
L9	1	S	L3 AND L8
		E	SARATOGA X J/AU
		E	JIAN X/AU
		E	JIANG X/AU
L10	3488	S	E3
		E	BECHA S D/AU
L11	126	S	E5
		E	YANG Y G/AU
L12	458	S	E3
		E	SWARNAKER A/AU
L13	3	S	E4
		E	BULLOCH S A/AU
L14	52	S	E3-E6
L15	4093	S	L10 OR L11 OR L12 OR L13 OR L14
L16	0	S	L2 AND L15
L17	0	S	L8 AND L15
L18	24	S	L15 AND TRANSFERASE?
L19	17	DUP REM	L18 (7 DUPLICATES REMOVED)

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 20070178438 A1		US-PGPUB	20070802	43	Apolipoprotein c-1 induced apoptosis
2	US 20070173467 A1		US-PGPUB	20070726	183	Rna interference mediated inhibition of cholesteryl ester transfer protein (cetp) gene expression using short interfering nucleic acid (sina)
3	US 20060142226 A1		US-PGPUB	20060629	181	RNA interference mediated inhibition of cholesteryl ester transfer protein (CETP) gene expression using short interfering nucleic acid (siNA)
4	US 20050171040 A1		US-PGPUB	20050804	177	RNA interference mediated inhibition of cholesteryl ester transfer protein (CEPT) gene expression using short interfering nucleic acid (siNA)
5	US 20020048572 A1		US-PGPUB	20020425	31	Treatment of hypertriglyceridemia and other conditions using LXR modulators

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 20070037797 A1		US-PGPUB	20070215	29	Method of reducing the risk of adverse cardiovascular (CV) events associated with the administration of pharmaceutical agents which favor CV events
2	US 20050209837 A1		US-PGPUB	20050922	96	Bactericidal/permeability-increasing protein: crystallization, x-ray diffraction, three-dimensional structure determination, rational drug design and molecular modeling or related proteins
3	US 20040014153 A1		US-PGPUB	20040122	168	Bactericidal/permeability-increasing protein: crystallization, x-ray diffraction, three-dimensional structure determination, rational drug design and molecular modeling of related proteins
4	US 20030040002 A1		US-PGPUB	20030227	27	Method for providing current assessments of genetic risk
5	US 6093573 A		USPAT	20000725	158	Three-dimensional structure of bactericidal/permeability-increasing protein (BPI)

6	US 5846720 A		USPAT	19981208	95	Methods of determining chemicals that modulate expression of genes associated with cardiovascular disease

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
7	US 5580722 A		USPAT	19961203	93	Methods of determining chemicals that modulate transcriptionally expression of genes associated with cardiovascular disease

	L #	Hits	Search Text
1	L1	48	ester adj transferase$2
2	L2	1016612	clon$3 or express$3 or recombinant
3	L3	5	l1 same l2
4	L4	89946	JIANG BECHA BULLOCH YANG SWARNAKAR
5	L5	7	l1 and l4

	L #	Hits	Search Text
1	L1	48	ester adj transferase$2
2	L2	1016612	clon$3 or express$3 or recombinant
3	L3	5	l1 same l2
4	L4	89946	JIANG BECHA BULLOCH YANG SWARNAKAR
5	L5	7	l1 and l4
6	L6	4	"LIPAM-6"